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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
07/431,533	11/03/89	MORTON	P-P310462

EXAMINER

HM22/0621

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ART UNIT	PAPER NUMBER
DAVIS, M	73

DATE MAILED: 1642 06/21/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on 2-13-00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 19, 62-66, 69-70, 72-79 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 19, 62-66, 69-70, 72-79 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19, 62-66, 69-70, and 72-79 are being examined.

REJECTION UNDER 35 USC 101, DOUBLE PATENTING

Rejection under 35 USC 101, double patenting of claims 19, 62-66, 69-70, 72-29 remains, because the Office has not received the terminal disclaimer.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH, NEW REJECTION

1. Claims 19, 62-66, 69-70, 72-79 are indefinite because claims 62 and 73 recite the language "substantially", which does not set forth the metes and bounds of the patent protection desired. The term "substantially" in the claims is a relative term which renders the claims indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

2. Claim 72 is indefinite because it is not clear that the enhancement of about 2- to 5-fold is compared to what.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT, NEW REJECTION

Claims 73-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection has been set forth for previous claims 19 and 47 of paper No: 23.

Claims 73-79 are drawn to a pharmaceutical composition comprising a urinary tumor associated antigen (UTAA).

Inherent in a pharmaceutical composition is the *in vivo* use thereof, i.e. treatment of cancer using UTAA.

The specification discloses production of antibodies in patients injected with irradiated tumor cells. In the amendment of 09/03/97, paper No: 37, applicant submitted a reference by Hunt et al, 1992, wherein administration of isolated UTAA to baboons generates production of polyclonal antibodies against UTAA, which could elicit complement-dependent lysis of tumor cells *in vitro*. The specification does not disclose treating a patient by administrating UTAA. The claims however encompass treating cancer patients by administering isolated UTAA. It is

unpredictable that injection of a purified tumor antigen into a patient would be sufficient for treating a tumor. Stites et al, 1993, (eds), Medical Immunology, Appleton & Lange, p. 637 teach that direct immunization with tumor protein generally has limited or no apparent efficacy. Urban et al, 1992, p.634, as recited in the Office action of paper No:23, on 12/01/93, teach that tumors may not produce sufficient amount of critical costimulatory factors at the tumor site to activate the responding CTLs, and that antigen expression in the absence of costimulatory factors may tolerize T cells to the tumor-specific molecule. The immunogenic T-cell epitopes may be subdominant, cryptic, or otherwise weakly antigenic. Local environment at the tumor site could prevent terminal T-cell differentiation. Thus production of antibodies against UTAA in healthy baboons could not be correlated with production of antibodies in patients, due to difference in *in vivo* environment of healthy baboons and the patients. Although injection of UTAA into healthy baboons produces antibodies against UTAA, one of skill in the art cannot predict that there would be sufficient amount of antibodies produced for sufficient periods of time in cancer patients, especially melanoma patients. Morton et al, 1989, as recited by applicant on paper NO:35, on 02/13/1995, teach that although antibodies could be elicited in patients by administering whole melanoma cells containing UTAA, many patients do not respond or have transient antibody response, due to suppressor T cell activity (p.670). In addition, Morton et al teach that melanoma treatment is complex, because humoral responses of individual patients are heterogenous, and that expression of tumor antigens is hetergenous on tumor cells of different patients (p.680). The specification does not teach how to avoid suppressor T cell activity when administering the

isolated UTAA. The specification does not teach how to use the claimed isolated UTAA to treat a cancer patient. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed isolated UTAA when injected into a cancer patient, with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention

One cannot extrapolate the teaching of the specification to the claims because it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the isolated UTAA could be successfully used in treating cancer. Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors

(p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2). It is clear that based on the state of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the isolated UTAA could be successfully used in treating cancer. In addition, Hartwell et al (Science, 1197, 278:1064-1068) teach that an effective chemotherapeutic must selectively kill tumor cells, that most anticancer drugs have been discovered by serendipity and that the molecular alterations that provide selective tumor cell killing are unknown and that even understanding the detailed molecular mechanism by which a drug acts often provides little insight into why the treated tumor cell dies (para bridging pages 1064-1065) and Jain (cited supra) specifically teaches that systemic treatment typically consists of chemotherapeutic drugs that are toxic to dividing cells (p. 58, col 2, para 2). In addition, anti-tumor agents and those that prevent, reduce, retard or eliminate secretion of metastatic promoters, must accomplish several tasks to be effective. They must be delivered into the circulation that supplies the tumor or metastatic promotor producing cells and interact at the

proper site of action and must do so at a sufficient concentration and for a sufficient period of time. It is clear, as disclosed above that the specification does not teach how to make/use a formulation with a targeting molecule. Also, the target cell must not have an alternate means of survival despite action at the proper site for the drug. In addition variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The formulation may be inactivated *in vivo* before producing a sufficient effect, for example, by degradation, immunological activation or due to an inherently short half life of the formulation. In addition, the formulation may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells and tissues where the formulation has no effect, circulation into the target area may be insufficient to carry the formulation and a large enough local concentration may not be established. The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed isolated UTAA with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

REJECTION UNDER 35 USC 103, NEW REJECTION

Claims 19, 62-66, 69-70, and 72-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Euhus et al., *supra*, in view of Exley, AR, 1990, Cytokine, 2(5): 353-6, Rote,

NS et al., 1980, J Surgical Research, 29: 18-22, or Finck SJ et al, 1982, J Surgical Oncology, 21: 81-86, Pharmacia Fine Chemicals, Gel filtration, Theory and practice, 1980, pages 4, 14, 26-27, Pharmacia fine Chemicals, Ion exchange chromatography, Principles and methods, 1980, pages 3-7, 43-47, Ljungquist, S, 1977, JBC, 252(9): 2808-2814, Goldenberg, 1982, US 4,348,376, further in view of Hofmann, HD, 1987, J Neurochemistry, 48(5): 1425-33.

Claims 19, 62-66, 69-70, and 72-79 are drawn to an isolated Urinary Tumor Associated Antigen (UTAA) subunit, which after reduction by beta-mercaptoethanol and separation by SDS-polyacrylamide gel electrophoresis (SDS-PAGE), exhibits a molecular weight of about 90 to 100 kD. Said UTAA is purified at least about 100-fold, or 105-fold over UTAA found in urine, and is present as at least about 0.6% of total protein in the original composition. The specification discloses that said degree of purification is obtained after purification of urine from a patient through a Sephacryl S-200 column (p22). The claims 69-70 are further drawn to the claimed UTAA, which is about 95% or 99.5% free of immunoglobulin. The specification discloses that after purification via DEAE-sephacel column, and absorption with rabbit anti-human IgG immunobeads to remove IgG, UTAA isolated from a patient serum is 95% to 99.5% free of IgG (p.34). Claims 19, 62-66, 69-70, and 72-79 are also drawn to a pharmaceutical composition comprising said purified UTAA, and a pharmaceutical buffer, wherein said UTAA is present as at least about 0.63 ug/ml, or 1.4 ug/ml, or 36 ug/ml, or 40 ug/ml, or 100 ug/ml, or 200 ug/ml of buffer. Claims 19, 62-66, 69-70, and 72-79 are further drawn to a method for inducing or

enhancing in a subject the production of antibodies reactive with UTAA, comprising administering said purified UTAA. The observed enhancement of antibody production is about 2- to 5-fold.

Claims 73-79 recite the claimed UTAA, formulated as a pharmaceutical composition. However, this limitation is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claims with the prior art. Claims read on the ingredient per se, which is UTAA.

The teaching of Euhus et al, Exley et al, Rote et al, Finck et al, Pharmacia Fine Chemicals, Ljungquist, and Goldenberg has been set forth in the previous Office action, paper No: 68

Euhus et al. teach the isolation of urinary tumor asssociated antigen (U-TAA) from sera of melanoma patients. Euhus et al. also teach that because said antigen was detected in the urine of melanoma patients, using autologous and allogeneic antibody in ELISA, it was termed urinary tumor asssociated antigen . A monoclonal antibody to U-TAA is developed, and used in ELISA to detect U-TAA. Said U-TAA is isolated by dye ligand, and gel filtration chromatography, and DEAE anion exchange chromatography or 4.5% polyethylene glycol precipitation. The free U-TAA in serum has a molecular mass of 620 kD, which is separated into four bands in SDS-PAGE; two of which, 142 kD and 111 kD, correspond to those present in U-TAA in urine. The isolated U-TAA is free of IgG and IgM. Euhus et al. further teach that pure U-TAA antigen will provide valuable reagents for the immunoprognosis of human melanoma.

Euhus et al. do not teach that UTAA is purified at least about 100-fold, or 105-fold over UTAA found in urine, and is present as at least about 0.6% of total protein in the original

composition. Euhus et al. do not teach that said UTAA is about 95% or 99.5% free of immunoglobulin. Euhus et al. do not teach a pharmaceutical composition, wherein said UTAA is present as at least about 0.63 ug/ml, or 1.4 ug/ml, or 36 ug/ml, or 40 ug/ml, or 100 ug/ml, or 200 ug/ml of buffer. Euhus et al. do not teach a method for inducing or enhancing in a subject the production of antibodies reactive with UTAA, comprising administering said purified UTAA, wherein the observed enhancement of antibody production is about 2- to 5-fold.

Exley et al teach how to perform enzyme-linked immunosorbent assay or ELISA.

Rote et al. teach tumor-associated antigens detected by autologus sera in urine of patients with solids neoplasms, using complement fixation assay. Unlike other tumor-related urinary antigens, the antigens taught by Rote et al induce a complement fixing antibody in the host, are heat stable at 100^0 C for 60 min. Said antigens are comprised of molecules of about $1x\ 10^6$ daltons, which could be dissociated into smaller subunits by treatment with 6 M urea.

Finck et al teach tumor-associated antigens found in urine of patient with colon carcinoma. Said antigen could be detected with complement fixation assay, using autologous serum as the antibody source. Said antigen has a molecular weight of >100,000 dalton, and is heat stable at 100^0 C (p.85).

Pharmacia Fine Chemicals teach how to purify proteins using gel filtration and ion exchange chromatography. Pharmacia teaches that "the separation of proteins in gel filtration depends on the different abilities of the various sample molecules to enter pores which contain the stationary phase. Very large molecules which never enter the stationary phase, move through the

chromatographic bed fastest" Smaller molecules are eluted in order of decreasing molecular size" (Gel filtration, page 4). The eluent is just a simple buffer solution, as shown in one example on figure 6, page 14 (Gel filtration). Furthermore, molecular weight standards are routinely used for calibrating the gel filtration column (Gel filtration, pages 26-27). It is well known in the art that molecular weight standards could be easily tagged with dye ligands for color detection on the column. Pharmacia also teaches methods of elution of proteins from ion exchange columns, including DEAE columns, using a continuous NaCL gradient (Ion exchange chromatography, pages 3-7, 43-47). Peaks of different proteins are separated by said continuous gradient elution, and thus could be detected.

Ljunquist teaches the purification of endonuclease IV by 3000-fold, using a combination of ammonium sulfate, gel filtration on Sephadex G-75, heat treatment, and DNA-cellulose.

US 4,348,376 teaches production of antibodies to the tumor antigen CEA, and the use of said antibodies for tumor localization and therapy.

Hofmann et al teach isolation of a protein, a neuronotrophic factor, using a combination of gel filtration method, preparative isoelectric focusing, and SDS-PAGE, wherein the protein is electrophoretically eluted from gel strips of SDS-PAGE (p.1427). The position of the gel strips could be determined by molecular weight standards. Using SDS-PAGE technique, the seminal vesicle-derived neuronotrophic factor (SVNF) could be completely separated from a closely associated protein, a nerve growth factor (NGF).

The art establishes that it was possible at the time the invention was made to isolate UTAA from sera of melanoma patients. Said UTAA is termed urinary tumor associated antigen because it is detected in urine of melanoma patients. A subunit of said UTAA from sera is 111 kD in SDS-PAGE, corresponding those present in UTAA in urine. Although 111 kD is not 90 to 100 kD, it is well known in the art that molecular weight determination by SDS-PAGE, at high molecular weight range, is not very accurate, and could easily vary by 10%. As also shown by applicant's own data, the molecular weight of the claimed UTAA varies by about 10%. Thus the 111 kD UTAA taught by Euhus et al. could have a similar molecular weight as the claimed UTAA. The art also teaches the protocols for isolating UTAA, i.e. by gel filtration, and DEAE anion exchange columns, and elution of proteins from SDS-PAGE. Although the abstract by Euhus et al does not describe in detail how to isolate UTAA using gel filtration, and DEAE anion exchange columns, it is a routine protocol in the art, as shown in the handbooks Pharmacia, or Ljungquist. In other words, proteins of different sizes are separated by gel filtration, using a simple buffer solution; and different proteins are separated by a DEAE column, eluted as different protein peaks, using a continuous salt gradient elution. In addition, the art teaches how to isolate proteins from gel slices of SDS-PAGE, wherein the molecular weight of the gel slice could be determined by molecular weight standards in adjacent lanes. The art further teaches how to detect UTAA, i.e. either by ELISA, or by complement fixation test, using autologous or allogeneic sera of melanoma patients. Although the abstract by Euhus et al does not describe in detail how to perform ELISA, ELISA is a routine protocol in the art, as shown by Exley et al. Thus the eluted

peaks from gel filtration, DEAE column, or gel slices of SDS-PAGE could be detected by either ELISA or by complement fixation test, using autologous or allogeneic sera of melanoma patients.

Therefore, it would have been *prima facia* obvious to a person of ordinary skill in the art at the time the invention was made to purify UTAA from urine or serum samples of melanoma patients, using the purification methods taught by Euhus et al, wherein the details of said methods are taught by Pharmacia, Ljungquist, and Hofmann et al. It would have been obvious to use the ELISA detection methods taught by Euhus et al, wherein the details of said methods are taught by Exley et al, and the antibodies for detection are from autologous or alleogenic sera of melanoma patients, as taught by Rote et al, and Finck et al. It would have been obvious to combine the gel filtration, and DEAE purification methods taught by Euhus et al, with electrophoretic elution of UTAA from gel strips of SDS-PAGE, as taught by Hofmann et al, because of the following reasons: 1) Hofmann et al teach a combination of gel filtration, and SDS-PAGE gel elution methods for purifying a protein, wherein the SDS-PAGE step would further purify the protein from another protein, which is usually associated with the purified protein, and 2) Euhus et al teach that UTAA could be readily detected on SDS-PAGE, at molecular weights of 142 kD and 111 kD. The isolated UTAA, as taught by Euhus et al, would be the same as the claimed UTAA, which is isolated from urine and sera of melanoma patients, because urine and serum samples of melanoma patients could be used for UTAA isolation, wherein UTAA is originally found in urine of melanoma patients, and wherein the molecular weight (111 kD) of a subunit of UTAA taught by Euhus et al. is not significantly different from that of the claimed UTAA, having a molecular

weight from about 90 kD to about 100 kD. Furthermore, the urine and serum samples of melanoma patients, that one of ordinary skill in the art could use for UTAA purification, would be the same as those used by applicant, because there is no specific teaching in the claims and the specification concerning any specific properties of urine and serum samples from melanoma patients which are used for UTAA purification. Furthermore, UTAA isolated by the combination methods taught by Euhus et al, and Hofmann et al would be at least 95% or 99.5% free of immunoglobulin, because of the following reasons: 1) Euhus et al teach that the isolated UTAA is free of IgG and IgM, and 2) the gel slice containing UTAA at a molecular weight of 111 kD would not contain immunoglobulin, which is well known in the art to have a molecular weight of about 150 kD. Although Euhus et al. do not specifically teach the degree of purification of UTAA, i.e at least at about 0.6% of total protein, and 105-fold over UTAA found in urine, such degree of purification is expected, given similar protocols used by Euhus et al and applicant, i.e. a UTAA fraction obtained from purification of urine by gel filtration. Once UTAA is isolated, it would have been obvious to dilute it or to concentrate it to various concentrations in a buffer.

It would have been obvious to use UTAA for inducing or enhancing the production of antibodies reactive to UTAA, because Euhus et al suggest the use of the isolated UTAA for the immunoprognosis of human melanoma, and because it is well known in the art that tumor antigens are used for the production of antibodies, and antibodies to tumor are used for treating tumors (see for example, US 4,348,376). Furthermore, administering the same antigen UTAA is expected to give similar 2- to 5-fold enhancement in the production of antibodies reactive to UTAA,

because the specification does not disclose any specific method of production of antibodies which is different from routine methods of production of any antibody known in the art.

One of ordinary skill in the art would have been motivated to isolate UTAA from urine of melanoma patients, and to use said isolated UTAA for inducing or enhancing the production of antibodies reactive to UTAA, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to isolate UTAA from urine of melanoma patients, and to use said isolated UTAA for inducing or enhancing the production of antibodies reactive to UTAA for the immunoprognosis of melanoma.

ANSWERS TO APPLICANT'S ARGUMENTS

Applicant argues as follows:

1. The cited references only provide an invitation to try to reproduce the invention, to isolate something called UTAA. Using an autologous or allogenic serum from melanoma patients for identifying fractions eluted from gel filtration and DEAE columns, how would one know which fractions that react with the antibodies in the serum contain UTAA, because the serum contains several antibodies, besides antibodies to UTAA, much less how one could identify a patient that even contains such antigen.

2. It is improper that the Examiner argues inherency in 103 rejection for claims 63, 64, 66, 69 and 70, concerning the degree of purification. Euhus reports nothing regarding other immunoglobulin species, there could be have been 1-6% contamination with other Ig's.

Applicant's arguments set forth in paper No: 71 of 03/06/00 have been considered but are not deemed to be persuasive for the following reasons:

1. The positive fractions from gel filtration or DEAE columns, i.e. fractions that react with the antibodies in the serum, could be easily identified by SDS-PAGE, as taught by Euhus et al, wherein any fraction containing a protein at 110 kD under SDS-PAGE would contain UTAA. Furthermore, it is well known in the art that cancer patients, including those having melanoma, have tumor associated antigens in their urine, as taught by Rote et al, and Finck et al. The urine and serum samples of melanoma patients, that one of ordinary skill in the art could use for UTAA purification, would be the same as those used by applicant, because there is no specific teaching in the claims and the specification concerning any specific properties of urine and serum samples from melanoma patients which are used for UTAA purification.

2. UTAA isolated by the combination methods taught by Euhus et al, and Hofmann et al would be at least 95% or 99.5% free of immunoglobulin, because of the following reasons: 1) Euhus et al teach that the isolated UTAA is free of IgG and IgM, and 2) the gel slice containing UTAA at a molecular weight of 111 kD would not contain immunoglobulin, which is well known in the art to have a molecular weight of about 150 kD. In addition, the specification does not disclose any purification of UTAA from Ig's other than IgG and IgM, and the claims do not specify that UTAA is 95-99.5% free from Ig's other than IgG and IgM. Thus purification from Ig's other than IgG and IgM is not an issue for 103 rejection here. Furthermore, using the same starting sample, i.e. urine, and the same purification technique, i.e. gel filtration, it is expected that

the same degree of purification is obtained. That is, although Euhus et al. do not specifically teach the degree of purification of UTAA, i.e at least at about 0.6% of total protein, and 105-fold over UTAA found in urine, such degree of purification is expected, given similar protocols used by Euhus et al. and applicant.

UTAA isolated by one of ordinary skill in the art, using urine or serum from melanoma patients, and the combined techniques taught by prior art, would be the same as the claimed UTAA, for the following reasons: 1) both proteins are derived from the same source, i.e. urine or serum from cancer patients, 2) the samples are purified by the same gel filtration and DEAE methods, except for gel slice elution for further purification, 3) both proteins have similar molecular weight under SDS-PAGE, and similar degree of purification, *supra*.

The rejections over the declarations by Shively and Reisfeld have been set forth in the previous Office actions of paper No: 66, on 08/05/98 and No: 54, on 03/13/97.

All other previous rejections in previous Office actions are withdrawn. NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 9:30am to 3:30pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

May 31, 2000

Primary SUSAN UNGAR
PATENT EXAMINER